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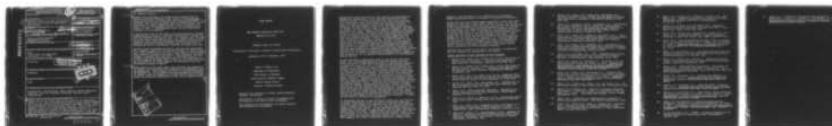
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CHEMICAL INDEX TO FITNESS (BIOCHEMICAL CORRELATES OF STRESS IN --ETC(U)
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20. ABSTRACT (Continue on reverse side if necessary and identify by block number)

During the 6th and final year of this contract we published a
report on our third neuroendocrine study of sleep, which examined
the secretion patterns of the posterior pituitary hormone, anti-
diuretic hormone, in normal young adult men. This is the first
reported study of the longitudinal secretion patterns of a
posterior pituitary hormone in human subjects, and it was found
that antidiuretic hormone was secreted episodically, like the
anterior pituitary hormones, but with no change in integrated

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plasma levels throughout the night nor any relation of the specific secretory episodes to any stages of sleep. In this study plasma levels of aldosterone and prolactin also were measured, both of which hormones showed increasing blood levels throughout the night, suggesting that these two hormones may play a role in the diminished amount of urine secreted by the kidney at night. A comprehensive report on this sleep study currently is in preparation.

A replication study of the effect of pharmacologically enhanced plasma prolactin levels on testosterone secretion in normal men also was performed during this year. The findings were the same, as in the first study reported last year, namely, that enhanced prolactin levels result in moderately enhanced testosterone secretion, which gives further evidence that prolactin plays an influential role in testosterone secretion in normal adult men.

Another project undertaken during the year was the development of a computer program for the variable analysis of scored sleep data, which permits the scoring of sleep stages by user-specified time intervals throughout the night. This program is important because it permits the computation of sleep variables for correlation with physiologic measures such as blood sampling; i.e., if blood samples are taken every 20 minutes, the sleep variables may be scored in 20 minute segments for correlation with the biochemical measures in blood.

Other aspects of this past year's work included the preparation of several invited chapters for textbooks of psychopharmacology and psychiatry. These studies are part of a continuing program of research into the biochemical and psychoendocrine correlates of stress, sleep and dreaming, and other central nervous system states in specialized populations as well as in normal subjects.

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FINAL REPORT

ONR CONTRACT NR108-912; NR202-004

(N00014-73-C-0127)

Chemical Index to Fitness

(Biochemical Correlates of Stress in Specialized Populations)

September, 1975 to November, 1976

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Contract work performed at Harbor General Hospital,
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During the 6th and final year of this contract we published the preliminary communication on the nocturnal secretion of antidiuretic hormone in normal young adult men (22), which was part of a large sleep study investigating the nocturnal secretion patterns of hormones influencing water and electrolyte balance. Using the same experimental design as in our other sleep studies, we sampled 8 normal subjects every 20 minutes throughout the night and assayed the blood samples for antidiuretic hormone, aldosterone, prolactin, and sodium. Whereas the levels of antidiuretic hormone did not increase during the night, both aldosterone and prolactin levels did increase during the hours of sleep, suggesting that these two hormones may play a role in the diminished amount of urine secreted by the kidney at night. The major report on this sleep study has been submitted for publication. We are pursuing the control of antidiuretic hormone by performing neuropharmacologic studies to elucidate which CNS neurotransmitter systems are involved in the control of this posterior pituitary hormone; a report has been submitted for publication which shows that CNS dopamine blockade with haloperidol results in increased plasma prolactin levels but has no effect on antidiuretic hormone levels, suggesting that dopamine is not an important neurotransmitter in antidiuretic hormone control.

We also performed a replication study of our initial work which showed that neuropharmacologically increased plasma prolactin levels result in a dose-related increase in testosterone secretion in normal adult men (20, 21). The second study utilized normal subjects on 4 separate test days, which were saline control, haloperidol-induced increased prolactin levels, intravenous infusion of human luteinizing hormone, and increased prolactin levels along with infused luteinizing hormone. This study not only replicated the first study but also examined the possibility of acute synergistic effects between prolactin and luteinizing hormone on testosterone secretion. Compared to saline control, testosterone secretion was again increased following the haloperidol-induced increases in plasma prolactin levels. Following the intravenous infusion of luteinizing hormone, testosterone levels were clearly increased, but were not further increased when prolactin levels were stimulated along with the infused luteinizing hormone. Therefore, while the first study was replicated in that increased prolactin levels alone resulted in a higher plasma testosterone level than saline control, no synergism was demonstrated between increased prolactin and luteinizing hormone levels on testosterone secretion. A report on this study is currently in preparation.

To investigate the day to day variability within the same subjects in plasma testosterone levels and urine testosterone secretion, 3 subjects were studied on 6 separate days each, by blood sampling every 30 minutes between 0900 and 1700, and by complete urine collections during this period. It was demonstrated that there was a coefficient of variation of approximately 25% in plasma testosterone levels across the 6 days. Whereas urine testosterone levels did not correlate at all with plasma testosterone levels, urine testosterone levels did correlate extremely highly with urine volume. This suggests that urine testosterone excretion is highly volume

dependent, and therefore is not a substitute for integrated plasma testosterone levels in studies of testosterone secretion.

During this past year several papers appeared in print which were in press at the time of last year's report (20, 21, 22, 24, 26). Other work undertaken during this past year includes the preparation of two invited chapters on psychoneuroendocrinology (30, 32) and the development of a computer program for the variable analysis of scored sleep data (31). This computer program permits the user to specify the length of the time interval in minutes for which sleep stage data will be compiled throughout the night. This program is very useful for the correlation of sleep staging with biochemical and physiological measures; e.g., if blood sampling is done every 20 minutes throughout the night, the program user can specify the scoring of sleep stage variables by 20 minute epochs throughout the night, so that the sleep stage measures can be correlated with the biochemical measures.

Although this contract is now ended, the reports in preparation will be submitted for publication in the future.

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